CHAPTER 11

NEUROLOGICAL ASSESSMENT

INTRODUCTION

Background

Neurological signs and symptoms, as distinguished from overt diagnosable neurological disease, have been consistently associated with industrial exposure to chlorophenols, phenoxy herbicides, and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Thus, the neurological system comprises a major examination focal point in all dioxin morbidity studies. This report separates central and peripheral neurological status from "neurobehavioral" parameters, which are discussed in Chapter 12, Psychological Assessment.

Based on animal experiments, neurotoxicity can be attributed to the compounds 2,4-D and TCDD. For low to moderate doses, both central and peripheral acute effects occur but appear to be reversible.[1-3] The effects of 2,4-D are presumably due to disruption in the neuromuscular transport system of organic acid anions.[4] A variety of 2,4-D experiments in several animal species generally shows a wide range of neural pathology including electroencephalographic (EEG) desynchronization, demyelination, myotonia, loss of coordination, and uncontrolled motor activity. Recent work indicates that effects are related to specific 2,4-D esters or ester combinations.[5] One study indicated that intraperitoneal injection of 2,4-D is not toxic to peripheral nerves in rats.[6] No substantive data support the isolated neurotoxicity of 2,4,5-T.

Numerous case reports following accidental human exposures or suicide attempts with 2,4-D have shown a remarkable neurological parallel to the animal studies.[7-12] In particular, 2,4-D and TCDD have been implicated in a wide array of central neurological signs and symptoms, including headache, vomiting, dizziness, disorientation, sleep disturbance, stupor, memory loss, loss of coordination, and EEG abnormalities or alterations from a baseline tracing.[7-9,11,13-15] Peripheral abnormalities have included demyelination, acute degeneration of ganglion cells, temporary paralysis, anesthesia, hyperesthesia, paresthesia, neuralgic pain, numbness, tingling, muscle pain, muscle fasciculations, depressed or absent deep tendon reflexes, weakness, decreased nerve conduction velocities, "polyneuritis," and limb fatigue.[7-18] These peripheral signs and symptoms in industrial workers have received the generic diagnostic label "neurasthenia." Both the number and severity of symptoms tended to aggregate in individuals with chloracne as contrasted to those without chloracne.[13,18,19]

Studies of exposed populations have included those from Times Beach, Missouri, and Seveso, Italy. Soil levels at Times Beach ranged from 20 to 1,000 ppb of TCDD with exposure lasting up to 2 years.[20,21] Studies indicated no major peripheral nervous system disorders but did find significant increases in numbness of the hands or feet and persistent severe headaches.[21,22] At Seveso, no significant peripheral neuropathy was found (based on diagnostic criteria), but significant chemical and electrophysical signs of peripheral nervous system involvement were found.[23,24] Soil levels reached 4,000 ppb of TCDD and exposure periods were as long as 2 months.[20]

Numerous industrial exposures have been studied. Forty-five railroad workers clearing a chemical spill were exposed to 45 ppb of TCDD in 20,000 gallons of orthochlorophenol-crude in 1979. Forty-three were diagnosed with peripheral neuropathies based on multiple-criteria for diagnoses. Peripheral nervous system symptoms, tremors, and distonias of the hands developed in many cases a few years after exposures.[25] A 2,4,5-trichlorophenol (TCP) factory explosion in Nitro, West Virginia, in 1949, resulted in manifestations of peripheral neuropathy for up to 2 years, but nerve conduction studies in 1979 found no differences between the exposed and control group.[26,27] An explosion in 1953 at a BASF TCP plant in Ludwigshafen, Federal Republic of Germany, resulted in a high incidence of peripheral neuropathy.[20,25] A study of the factory workers in Seveso (unrelated to the explosion) diagnosed peripheral nerve fiber damage and polyneuropathy of the lower extremities.[25] Numerous other occupational exposure cases have reported neurological symptoms but no specific diagnoses were made.[20,25,26,28]

In general, there is consistency between the various case reports of neurasthenia and results from uncontrolled clinical studies. Of particular relevance is the consistency in findings from studies of industrial manufacturing and industrial accidents. This literature suggests that neurological impairment is caused directly by exposure to 2,4-D and TCDD. Not answered satisfactorily in the literature, however, are the issues of reversibilty of observed signs and symptoms, the long-term effects on health and quality of life, and exposure levels associated with the various symptoms. Because of the evidence that suggests that two of three Agent Orange ingredients can cause neurological "disease," it follows that significant exposure to Agent Orange could manifest neurological signs, symptoms, or sequelae.

More than 10 percent of Vietnam veterans who enlisted in the Veterans Administration (VA) Agent Orange Registry cited one or more symptoms of the neurasthenic complex.[29] The VA Registry is a comprehensive listing, predominantly of veterans reporting health impairments they feel are due to Agent Orange exposure. The Registry does not purport to be a scientific effort upon which cause-and-effect relationships can be established. Nonetheless, some individuals believe that the symptom array in the VA Registry is so compatible with case reports and numerator-oriented clinical studies that the veterans must, in fact, have suffered adverse health effects from their Vietnam service and presumed exposure to Agent Orange. Others point to the intense media attention to "Agent Orange symptoms" during the formation of the Registry, and presume that the veterans' complaints are largely due to "overreporting."

Clearly, only well-controlled, well-conducted epidemiologic studies of veterans known to have been exposed to Agent Orange can answer the question of cause and effect for illnesses, including the specific question of whether single or multiple neurologic signs and symptoms are also attributable to these exposures.

Baseline Summary Results

The 1982 Air Force Health Study (AFHS) neurological assessment consisted of questionnaire, physical examination, and electromyographic data obtained by examiners and technicians who were blinded to the group identity of each participant. The physical examination required an average of 30 minutes to complete. Those few individuals with positive rapid plasma reagin tests, a

screening serological test for syphilis, and those with peripheral edema were deleted from the statistical analyses. Analyses were adjusted for reported alcohol usage, exposure to insecticides and industrial chemicals, and glucose intolerance (diabetes).

Results of the questionnaire disclosed no significant group differences in reported neurological diseases. The physical examination did not reveal any statistically significant group differences in the function of the 12 cranial nerves. Peripheral nerve function was assessed by the quality of four reflexes (patellar, Achilles, biceps, and Babinski); muscle strength/bulk; and reaction to the stimuli of pin prick, light touch, and vibration. Other than a statistically significant increase ($p=0.03$) in Ranch Hand Babinski reflexes, significant group differences were not detected. The alcohol covariate demonstrated a marginal effect ($p=0.07$) on pin-prick reaction, while glucose intolerance had a strong influence on the patellar and Achilles reflexes and reactions to light touch and vibration.

Nerve conduction velocities were obtained by highly standardized methods on the ulnar nerve above and below the elbow and the peroneal nerve. The results for each segmental measurement were nearly identical in the Ranch Hand and Comparison groups. Conduction velocity showed highly significant inverse relationships to both alcohol (measured in drink-years) and glucose intolerance in almost all of the anatomic measurements. No group associations or interactions were detected with the covariates of industrial and degreasing chemicals and insecticides.

No significant group differences were detected in four measures of central neurological function (tremor, finger-nose coordination, modified positive Romberg's sign, or abnormal gait). Alcohol usage was significantly associated with the presence of tremor, and glucose intolerance was highly correlated to abnormal balance and the presence of tremor.

Of a total of 84 exposure index analyses on the dependent variables, 3 were statistically significant but were either nonlinear or biologically implausible. In summary, the detailed neurological examination and assessment in 1982 did not reveal statistically significant increases in abnormalities in the Ranch Hands, nor were consistent dose-response relationships noted for herbicide exposure. The classical neurological effects of alcohol ingestion and diabetes were repeatedly observed in the neurological evaluations.

1985 Followup Study Summary Results

The 1985 AFHS neurological examination did not include the measurements of nerve conduction velocities but otherwise repeated the format of the Baseline examination. The questionnaire maintained a historical focus on neurasthenia through five questions for the 1982-1985 interval.

With this similarity in examination and questionnaire, the dependent variables of the analyses were almost identical to those of the Baseline study; however, the number of covariates was slightly increased. Diabetic status was trichotomized: Individuals reporting a history of diabetes (unverified) and individuals exhibiting glucose intolerance with postprandial glucose levels greater than or equal to 200 mg/dl were classified as diabetic, participants with glucose levels of at least 140 mg/dl but less than 200 mg/dl were classified as impaired, and participants with glucose levels less than

140 mg/dl were classified as normal. Race was included as a covariate, and lifetime alcohol use was updated on the basis of enhanced information from the 1985 questionnaire.

Interval questionnaire data (1982 through 1985) on neurological illneses, verified by medical records, revealed no significant group differences. These data were added to verified Baseline historical information to assess possible differences in the lifetime experience of neurological disease. Again, there was no significant difference between the Ranch Hands and Comparison groups.

The detailed neurological examination evaluated neurological integrity in three broad areas: cranial nerve function, peripheral nerve status, and central nervous system (CNS) coordination.

Assessment of the 12 cranial nerves was based on the measurement of 15 variables. Two summary indices were constructed. Neither the unadjusted nor adjusted analyses disclosed any statistically significant group differences, although two variables (speech and tongue position) were of borderline significance, with Ranch Hands faring worse than Comparisons. One of the two cranial nerve summary indices was marginally significant, again with the Ranch Hands at a slight detriment. In contrast to the Baseline examination, there was no significant group difference in Babinski reflex.

The unadjusted and adjusted analyses of peripheral nerve function, as measured by eight variables (four reflexes, three sensory determinations, and muscle mass), did not reveal significant group differences.

Coordination was evaluated by four measurements and a constructed summary variable. Hand tremor was found to be of borderline significance, with the Ranch Hands faring slightly worse than the Comparisons. The CNS summary index showed a significant detriment to the Ranch Hands.

The exposure analyses for neurological variables with reasonable counts of abnormalities showed only occasional statistically significant results. No consistent pattern with increasing exposure was evident for any occupational category of the Ranch Hand group.

In a longitudinal analysis of the Romberg sign and the Babinski reflex, only the Babinski reflex revealed a significant difference between the Baseline and 1985 followup examination, with the Ranch Hands converting from significant adverse findings at Baseline to favorable nonsignificant findings at the followup examination.

Overall, the 1985 followup examination findings are quite similar to the Baseline findings. However, several distinct patterns were evident from the analyses: (1) The followup examination detected substantially fewer abnormalities for almost all measurement variables; (2) the decrease in abnormalities was similar in both groups; (3) most of the covariate effects were expected, although exceptions were evident; (4) the adjusted analyses were uniformly similar to the unadjusted analyses; (5) a significant result was found for the constructed CNS summary variable and a marginally significant result was found for the constructed cranial nerve index excluding range of motion; and (6) although statistical significance at the pre-assigned α-level of 0.05 was not achieved for any of the measurement variables, abnormalities tended to cluster in the Ranch Hand group.

Of the three group-by-covariate interactions in the adjusted analyses, only one, a borderline group-by-insecticide exposure interaction for hand tremor, where Ranch Hands exposed to insecticides had a marginally significant adverse effect, was of probable biologic significance.

In conclusion, none of the 27 neurological variables demonstrated a significant group difference, although several showed an aggregation of abnormalities in the Ranch Hand group, which merit continued surveillance. Historical reporting of neurological disease was equal in both groups. None of the exposure analyses revealed dose-response patterns in the Ranch Hand occupational categories. The longitudinal analyses disclosed a favorable reversal of significant Babinski reflex abnormalities at Baseline to non-significant findings at the 1985 followup examination for the Ranch Hands. The similarity in results between unadjusted and adjusted statistical tests was evidence of group equality for the traditionally important neurological covariates of age, alcohol, and diabetes. Of three group-by-covariate interactions in the adjusted analyses, only the group-by-insecticide exposure interaction for hand tremor was biologically plausible.

Parameters of the 1987 Neurological Assessment

Dependent Variables

The 1987 neurological assessment was primarily based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases.

Questionnaire Data

Data on all major health conditions since the date of the last health interview were collected during the 1987 health interview. All affirmative histories were subjected to medical records verification. The verified information was used to update the health status of each study participant. The neurological diseases and disorders were classified into six International Classification of Disease (ICD) categories: inflammatory diseases, hereditary and degenerative diseases, peripheral disorders, disorders of the eye, disorders of the ear, and other disorders. The analyses of questionnaire information in the 1987 assessment were based on verified data only. Each of the six variables was coded as yes/no.

Participants with positive serological tests for syphilis were excluded from all analyses of these neurological variables, as well as participants with a verified pre-SEA history of these disorders.

Physical Examination Data

During the physical examination, assessments were made of cranial nerve function, peripheral nerve status, and CNS coordination processes.

The analysis of cranial nerve function was based on the following 17 variables: smell, visual fields, light reaction, ocular movement, facial

sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, neck range of motion, cranial nerve index, and the index excluding neck range of motion. All of these variables were scored as normal/abnormal except jaw clench, which was scored as symmetric/deviated. Left and right determinations were combined to produce a single normal/abnormal result, where normal indicates that both left and right determinations were normal. The cranial nerve index was created by combining responses for the 15 cranial nerve parameters into a single index, which was classified as normal if all parameters were normal. An index was also created excluding the hypoglossal nerve (neck range of motion).

Peripheral nerve status was assessed by light pin prick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), vibratory sensation as measured at the ankle with a tuning fork of 128 Hz, three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. Muscle status was a constructed variable using data on bulk, tone of upper and lower extremities, strength of distal wrist extensors, ankle/toe flexors, proximal deltoids, and hip flexors. Muscle status was classified as normal if all of the components were normal. The reflexes were coded as normal if they were sluggish, active, or very active; reflexes that were classified as absent, transient clonus, or sustained clonus were coded as abnormal for the analyses.

The evaluation of CNS coordination processes was based on the analysis of the following variables: tremor, coordination, Romberg sign, gait, and CNS index. Multiple determinations were combined to form a single result, which was normal if all determinations were normal. Coordination was an index defined as normal if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation/supination of hands, and rapid patting were normal. The CNS index was based on tremor, coordination, Romberg sign, and gait; this index was coded as normal if all four of the components were normal.

Participants with positive serological tests for syphilis were excluded from all analyses of these neurological variables. In the analysis of corneal reflex, participants who did not remove contact lenses and had no reflex were excluded. Participants with peripheral edema were excluded from the analyses of pin prick, light touch, and ankle vibration.

Covariates

The effects of age, race, occupation, lifetime alcohol history, current alcohol use, diabetic class, insecticide exposure, industrial chemical exposure, and degreasing chemical exposure were examined in the neurological assessment based on the physical examination variables, both in pairwise associations with the dependent variables and in adjusted statistical analyses. The exposure to insecticides, industrial chemicals, and degreasing chemicals covariates represents lifetime exposure based on self-reported questionnaire data.

The lifetime alcohol history and current alcohol use covariates were based on self-reported information from the questionnaire. For lifetime alcohol history, the respondent's average daily alcohol consumption was determined for various drinking stages throughout his lifetime, and an

estimate of the corresponding total number of drink-years (1 drink-year is the equivalent of drinking 1.5 ounces of 80-proof alcoholic beverage per day for 1 year) was derived. The current alcohol use covariate was based on the average drinks per day for the month prior to completing the questionnaire.

Age was treated as a continuous variable for all adjusted analyses, but was categorized for the covariate tests of association, and to explore exposure index-by-age interactions. Lifetime alcohol history and insecticide exposure were categorized for all analyses. Current alcohol use, degreasing chemical exposure, and industrial chemical exposure were categorized for the covariate tests of association, but because results for these analyses were either not significant or the associations were inconsistent with the expected effect, they were generally not used for the adjusted analyses (the only exception being that degreasing chemical exposure was used for the adjusted analysis of the cranial nerve index without neck range of motion). Results of the tests of association for these three covariates are presented in Table H-1 of Appendix H.

Relation to Baseline and 1985 Followup Studies

Except for other neurological disorders and the neurological summary indices, the same variables analyzed for the 1987 followup study were analyzed in the Baseline and 1985 followup studies. Other neurological disorders, cranial nerve indices with and without neck range of motion, and the CNS index were variables added to the analysis in the 1985 followup.

The neurological longitudinal analyses were based on the cranial nerve index and the CNS index. The Scripps Clinic and Research Foundation (SCRF) conducted both the 1985 and 1987 neurological examinations. To enhance the comparability, the longitudinal assessment contrasted group differences between the 1985 and 1987 followup examinations.

Statistical Methods

The basic statistical analysis methods used in the neurological assessment are described in Chapter 7.

Table 11-1 summarizes the statistical analyses performed for the 1987 neurological assessment. The first part of this table lists the dependent variables analyzed, data source, data form, cutpoints, candidate covariates, and statistical analysis methods. The second part of this table provides a description of candidate covariates examined. In the interest of space, abbreviations are used extensively in the body of the table and are defined in footnotes.

Some participants had missing dependent variable or covariate data. Consequently, these individuals could not be included in all analyses. Table 11-2 summarizes the number of participants with missing data, and the number who were excluded from analyses for medical reasons, by group and variable.

TABLE 11-1.

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Inflammatory Diseases	Q-V	D	Yes No	--	UC:FT
Hereditary and Degenerative Diseases	Q-V	D	Yes No	--	UC:FT
Peripheral Disorders	Q-V	D	Yes No	--	UC:FT
Disorders of the Eye	Q-V	D	Yes No	--	UC:FT
Disorders of the Ear	Q-V	D	Yes No	--	UC:FT
Other Neurological Disorders	Q-V	D	Yes No	--	UC:FT
Smell	PE	D	Abnormal Normal	--	UC:FT, UE:CS,FT
Visual Fields	PE	D	Abnormal Normal	--	UC;FT UE:CS,FT
Light Reaction	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Ocular Movement	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Facial Sensation	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Corneal Reflex	PE	D	Abnormal Normal	--	--
Jaw Clench	PE	D	Deviated Symmetric	--	UC:FT UE:CS,FT
Smile	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT

TABLE 11-1. (continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Palpebral Fissure	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Balance	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Gag Reflex	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Speech	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Tongue Position Relative to Midline	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Palate and Uvula Movement	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Neck Range of Motion	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Cranial Nerve Index	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR L:OR
Cranial Nerve Index Without Range of Motion	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Pin Prick	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 11-1. (continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Light Touch	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Muscle Status	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Vibration	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Patellar Reflex	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Achilles Reflex	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Biceps Reflex	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Babinski Reflex	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Tremor	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

TABLE 11-1. (continued)

Statistical Analysis for the Neurological Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analyses
Coordination	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Romberg Sign	PE	D	Abnormal Normal	--	UC:FT UE:CS,FT
Gait	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR
Central Nervous System (CNS) Index	PE	D	Abnormal Normal	AGE,RACE, OCC,DRKYR, ALC,DIAB, INS,IC,DC	UC:FT AC:LR CA:CS,FT UE:CS,FT AE:LR

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born >1942 Born 1923-1941 Born ≤1922
Race (RACE)	MIL	D	Black Nonblack
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew

TABLE 11-1. (continued)

Statistical Analysis for the Neurological Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Diabetic Class (DIAB)	LAB/Q-V	D	Diabetic: past history or ≥200 mg/dl glucose Impaired: ≥140-200 mg/dl glucose Normal: <140 mg/dl glucose
Current Alcohol Use (ALC) (drinks/day)	Q-SR	D/C	0-1 >1-4 >4
Lifetime Alcohol History (DRKYR) (drink-years)	Q-SR	D/C	0 >0-40 >40
Industrial Chemical Exposure (IC)	Q-SR	D	Yes No
Insecticide Exposure (INS)	Q-SR	D	Yes No
Degreasing Chemical Exposure (DC)	Q-SR	D	Yes No

Abbreviations:

Data Source:
LAB--1987 SCRF laboratory results
MIL--Air Force military records
PE--1987 SCRF physical examination
Q-SR--1987 NORC questionnaire (self-reported)
Q-V--1987 NORC questionnaire (verified)

Data Form:
D--Discrete analysis only
D/C--Appropriate form of analysis (either discrete or continuous)

Statistical Analyses:
UC--Unadjusted core analyses
AC--Adjusted core analyses
CA--Dependent variable-covariate associations
UE--Unadjusted exposure index analyses
AE--Adjusted exposure index analyses
L--Longitudinal analyses

Statistical Methods:
CS--Chi-square contingency table test
FT--Fisher's exact test
LR--Logistic regression analysis
OR--Chi-square test on the odds ratio

TABLE 11-2.

Number of Participants Excluded and With Missing Data for the Neurological Assessment by Group

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
Smell	DEP	0	1	1
Visual Fields	DEP	0	4	4
Light Reaction	DEP	0	4	4
Ocular Movement	DEP	0	3	3
Facial Sensation	DEP	0	2	2
Corneal Reflex	DEP	9	9	18
Balance	DEP	0	2	2
Gag Reflex	DEP	1	0	1
Speech	DEP	0	1	1
Cranial Nerve Index	DEP	10	20	30
Cranial Nerve Index Without Range of Motion	DEP	10	20	30
Pin Prick	DEP	0	1	1
Light Touch	DEP	0	2	2
Muscle Status	DEP	2	3	5
Vibration	DEP	0	2	2
Patellar Reflex	DEP	0	3	3
Achilles Reflex	DEP	2	2	4
Babinski Reflex	DEP	0	2	2
Coordination	DEP	1	3	4
Romberg Sign	DEP	0	2	2

TABLE 11-2. (continued)

Number of Participants Excluded and With Missing Data for the Neurological Assessment by Group

Variable	Analysis Use	Group: Ranch Hand	Group: Comparison	Total
Gait	DEP	1	2	3
CNS Index	DEP	1	3	4
Current Alcohol Use	COV	5	1	6
Lifetime Alcohol History	COV	10	3	13
Diabetic Class	COV	5	7	12
Pre-SEA Inflammatory Diseases	EXC	0	10	10
Pre-SEA Hereditary and Degenerative Diseases	EXC	1	1	2
Pre-SEA Peripheral Disorders	EXC	5	4	9
Pre-SEA Disorders of the Eye	EXC	3	1	4
Pre-SEA Otiotic Disorder	EXC	0	1	1
Pre-SEA Tympanic Membrane Disorder of the Ear	EXC	6	5	11
Pre-SEA Hearing Loss	EXC	4	9	13
Pre-SEA Other Neurological Disease	EXC	4	5	9
Syphilis	EXC	2	5	7
Pitting or Nonpitting Edema	EXC	22	30	52

Abbreviations: COV--Covariate (missing data)
DEP--Dependent variable (missing data)
EXC--Exclusion

Ranch Hand and Comparison Group Contrast

Questionnaire Variables

Unadjusted results for six categories of neurological diseases and disorders based on verified questionnaire data are seen in Table 11-3.

Inflammatory Diseases

No significant group difference was found for the incidence of post-Southeast Asia inflammatory diseases (ICD codes 32000-32600, p=0.270). Five Ranch Hands (0.5%) and two Comparisons (0.2%) were diagnosed with inflammatory disease.

Hereditary and Degenerative Diseases

For conditions classified as hereditary and degenerative diseases (ICD codes 33000-33700), the Ranch Hand group had significantly more verified cases than the Comparison group (5.4% vs. 3.5%, respectively; p=0.030). The estimated relative risk was 1.60 (95% C.I.: [1.07,2.39]). Examples of hereditary and degenerative disease include Parkinson's disease and benign essential tremor, among others. Among the Ranch Hands, 43 of 58 diagnoses of hereditary and degenerative disease (74%) were essential tremor, and 35 of the 46 diagnoses (75%) in the Comparisons were essential tremor.

Peripheral Disorders

The incidence of peripheral disorders (ICD codes 35000-35900) was not significantly different between groups (p=0.754).

Disorders of the Eye

The incidence of potentially neurological disorders of the eye (ICD codes 37800-37956) for Ranch Hands was not significantly different from the incidence for Comparisons (p=0.152).

Disorders of the Ear

External otitis (ICD codes 38010-38081), tympanic membrane disorder of the ear (ICD codes 38420-38500), and hearing loss (ICD codes 38900-38999) were examined. Only results for tympanic membrane disorder of the ear were tabulated. No signficant group difference was found for tympanic membrane disorder of the ear (p=0.672). The incidence of external otitis was 12.1 percent for Ranch Hands versus 12.4 percent for Comparisons (p=0.886). The incidence of hearing loss was not significantly different between the Ranch Hand and Comparison groups (73.0% vs. 74.7%, respectively; p=0.384).

TABLE 11-3.

Unadjusted Analysis for Neurological Disease Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Inflammatory Disease	n	993		1,284			
	Number/%						
	Yes	5	0.5%	2	0.2%	3.24 (0.63,16.76)	0.270
	No	988	99.5%	1,282	99.8%		
Hereditary and Degenerative Disease	n	992		1,293			
	Number/%						
	Yes	54	5.4%	45	3.5%	1.60 (1.07,2.39)	0.030
	No	938	94.6%	1,248	96.5%		
Peripheral Disorders	n	988		1,290			
	Number/%						
	Yes	140	14.2%	190	14.7%	0.96 (0.76,1.21)	0.754
	No	848	85.8%	1,100	85.3%		
Disorders of the Eye	n	990		1,293			
	Number/%						
	Yes	173	17.5%	196	15.2%	1.19 (0.95,1.48)	0.152
	No	817	82.5%	1,097	84.8%		
Tympanic Membrane Disorder of the Ear	n	987		1,289			
	Number/%						
	Yes	49	5.0%	58	4.5%	1.11 (0.75,1.64)	0.672
	No	938	95.0%	1,231	95.5%		

TABLE 11-3. (continued)

Unadjusted Analysis for Neurological Disease Variables by Group

Variable	Statistic	Group		Est. Relative Risk (95% C.I.)	p-Value
		Ranch Hand	Comparison		
Other Neurological Disorders	n	989	1,289		
	Number/%				
	Yes	213 21.5%	263 20.4%	1.07 (0.87,1.31)	0.542
	No	776 78.5%	1,026 79.6%		

Other Neurological Disorders

There was no significant group difference in the incidence of other neurological disorders (ICD codes 34000-34900, p=0.542).

Physical Examination Variables

Neurological parameters evaluated at the physical examination were grouped into 27 variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes. Group differences were assessed for these variables and for three additional summary indices. Unadjusted analyses were done for all variables with at least one abnormality, but adjusted analyses were only conducted for variables with a substantial number of abnormalites (>1.0% overall). Results of the covariate tests of association are summarized in Table H-1 of Appendix H. Results for stratified analyses to explore group-by-covariate interactions are presented in Table H-2.

Physical Examination Variables: Cranial Nerve Function

Group contrasts to assess cranial nerve function were examined for 17 variables, including two summary indices. Unadjusted and adjusted analyses were done for palpebral fissure, neck range of motion, the cranial nerve index, and the cranial nerve index without neck range of motion. Because there were few abnormalities, only unadjusted analyses were done for smell, visual fields, light reaction, ocular movement, facial sensation, jaw clench, smile, balance, gag reflex, speech, tongue position relative to midline, and palate and uvula movement. No analysis was done for corneal reflex because there were no abnormalities. Tables 11-4 and 11-5 present results for the unadjusted and adjusted analyses, respectively.

For the 12 variables with few abnormalities, a marginally significant group difference was found for balance (p=0.072). All four participants with an abnormal balance were Ranch Hands. Unadjusted results for the other variables did not reveal significant differences between groups. However, little power exists to detect significant group differences due to the presence of few abnormal responses.

Palpebral Fissure

The percentage of palpebral fissure abnormalities did not differ significantly between the Ranch Hand and Comparison groups for the unadjusted analysis (p=0.999).

Using pooled group data, palpebral fissure was not associated with any of the covariates.

A significant group-by-lifetime alcohol history interaction (p=0.040) was found for the adjusted analysis. A diabetic class-by-insecticide exposure interaction was used for adjustment (p=0.010). Stratified results did not reveal a significant group difference for any of the three lifetime alcohol history strata. A second adjusted analysis was done excluding the group-by-lifetime alcohol history interaction. No significant group difference

TABLE 11-4.

Unadjusted Analysis for Cranial Nerve Function Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Smell	n	993		1,293			
	Number/%						
	Abnormal	7	0.7%	13	1.0%	0.70 (0.28,1.76)	0.596
	Normal	986	99.3%	1,280	99.0%		
Visual Fields	n	993		1,290			
	Number/%						
	Abnormal	2	0.2%	7	0.5%	0.37 (0.08,1.78)	0.342
	Normal	991	99.8%	1,283	99.5%		
Light Reaction	n	993		1,290			
	Number/%						
	Abnormal	7	0.7%	9	0.7%	1.01 (0.38,2.72)	0.999
	Normal	986	99.3%	1,281	99.3%		
Ocular Movement	n	993		1,291			
	Number/%						
	Abnormal	7	0.7%	5	0.4%	1.83 (0.58,5.77)	0.452
	Normal	986	99.3%	1,286	99.6%		
Facial Sensation	n	993		1,292			
	Number/%						
	Abnormal	5	0.5%	7	0.5%	0.93 (0.29,2.94)	0.999
	Normal	988	99.5%	1,285	99.5%		
Jaw Clench	n	993		1,294			
	Number/%						
	Deviated	2	0.2%	0	0.0%	--	0.376
	Symmetric	991	99.8%	1,294	100.0%		

TABLE 11-4. (continued)

Unadjusted Analysis for Cranial Nerve Function Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Smile	n	993		1,294			
	Number/%						
	Abnormal	7	0.7%	10	0.8%	0.91 (0.35,2.40)	0.999
	Normal	986	99.3%	1,284	99.2%		
Palpebral Fissure	n	993		1,294			
	Number/%						
	Abnormal	14	1.4%	18	1.4%	1.01 (0.50,2.05)	0.999
	Normal	979	98.6%	1,276	98.6%		
Balance	n	993		1,292			
	Number/%						
	Abnormal	4	0.4%	0	0.0%	--	0.072
	Normal	989	99.6%	1,292	100.0%		
Gag Reflex	n	992		1,294			
	Number/%						
	Abnormal	1	0.1%	0	0.0%	--	0.868
	Normal	991	99.9%	1,294	100.0%		
Speech	n	993		1,293			
	Number/%						
	Abnormal	3	0.3%	2	0.2%	1.96 (0.33,11.73)	0.756
	Normal	990	99.7%	1,291	99.8%		
Tongue Position Relative to Midline	n	993		1,294			
	Number/%						
	Abnormal	2	0.2%	0	0.0%	--	0.376
	Normal	991	99.8%	1,294	100.0%		

TABLE 11-4. (continued)

Unadjusted Analysis for Cranial Nerve Function Variables by Group

Variable	Statistic	Group: Ranch Hand	Group: Comparison	Est. Relative Risk (95% C.I.)	p-Value
Palate and Uvula Movement	n	993	1,294		
	Number/%				
	Abnormal	1 0.1%	1 0.1%	1.30 (0.08,20.86)	0.999
	Normal	992 99.9%	1,293 99.9%		
Neck Range of Motion	n	993	1,294		
	Number/%				
	Abnormal	120 12.1%	139 10.7%	1.14 (0.88,1.48)	0.348
	Normal	873 87.9%	1,155 89.3%		
Cranial Nerve Index	n	983	1,274		
	Number/%				
	Abnormal	152 15.5%	185 14.5%	1.08 (0.85,1.36)	0.572
	Normal	831 84.5%	1,089 85.5%		
Cranial Nerve Index Without Range of Motion	n	983	1,274		
	Number/%				
	Abnormal	42 4.3%	57 4.5%	0.95 (0.63,1.43)	0.902
	Normal	941 95.7%	1,217 95.5%		

TABLE 11-5.

Adjusted Analysis for Cranial Nerve Function Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Palpebral Fissure	n	978	1,284	0.97 (0.47,1.99)**	0.928**	GRP*DRKYR (p=0.040) DIAB*INS (p=0.010)
Neck Range of Motion	n	993	1,294	1.13 (0.86,1.49)	0.377	AGE (p<0.001) RACE (p=0.003)
Cranial Nerve Index	n	978	1,268	1.05 (0.82,1.34)	0.691	AGE (p<0.001) RACE*DIAB (p=0.036)
Cranial Nerve Index Without Range of Motion	n	983	1,274	****	****	GRP*INS (p=0.008) AGE*DC (p=0.028)

GRP: Group (Ranch Hand, Comparison).

**Group-by-covariate interaction ($0.01<p\leq0.05$)--adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

****Group-by-covariate interaction ($p\leq0.01$)--adjusted relative risk, confidence interval, and p-value not presented.

(p=0.928) was found after adjusting for diabetic class-by-insecticide exposure.

Neck Range of Motion

The percentage of Ranch Hands with an abnormal neck range of motion was not significantly different from the corresponding percentage of Comparisons (p=0.348) in the unadjusted analysis.

Covariate tests of association revealed significant relationships between neck range of motion and age (p<0.001), race (p=0.001), occupation (p=0.001), and diabetic class (p<0.001). The percentage of participants with an abnormal range of motion increased dramatically with age (3.1%, 15.9%, and 37.4% for individuals born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). Nonblacks had relatively more abnormalities than Blacks (11.9% vs. 2.2%, respectively). Of the occupational cohorts, the highest percentage of abnormalities was found for officers (14.2%), followed by enlisted flyers (12.3%) and enlisted groundcrew (8.6%). For diabetic class, the percentages of abnormalities were 10.1 percent, 13.5 percent, and 18.4 percent for the normal, impaired, and diabetic categories, respectively.

No significant group difference was found (p=0.377) after adjusting for age (p<0.001) and race (p=0.003).

Cranial Nerve Index

No significant difference in the percentage of abnormalities between groups was detected (p=0.572) in the unadjusted analysis.

Age (p<0.001), race (p=0.024), occupation (p=0.024), and diabetic class (p=0.003) were significantly associated with this summary index; a marginal association with insecticide exposure was also noted (p=0.060). The patterns of the significant associations parallel those for neck range of motion. The percentage of abnormalities increased with age (6.5%, 19.8%, and 39.5% for participants born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). The percentage of abnormalities was higher for nonblacks (15.4%) than for Blacks (8.2%). Relatively more abnormalities were seen for the officer cohort (16.9%) and the enlisted flyer cohort (16.6%) than for the enlisted groundcrew cohort (12.7%). For diabetic class, participants classified as diabetic had a higher percentage of abnormalities (21.8%) than impaired individuals (17.2%) and normal individuals (13.6%). Participants exposed to insecticides had relatively more abnormalities than those not exposed to insecticides (16.0% vs. 13.0%, respectively).

The adjusted analysis did not reveal a significant group difference (p=0.691). Age (p<0.001) and race-by-diabetic class (p=0.036) were used for adjustment.

Cranial Nerve Index Without Neck Range of Motion

A significant difference between groups was not found for the unadjusted analysis (p=0.902).

The cranial nerve index without neck range of motion was marginally associated with age (p=0.058) and degreasing chemical exposure (p=0.056). The percentage of abnormalities increased with age (3.5%, 4.8%, and 8.6% for individuals born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). Individuals exposed to degreasing chemicals had a higher percentage of abnormalities (5.1%) than those who had never been exposed to degreasing chemicals (3.3%).

A significant group-by-insecticide exposure interaction (p=0.008) was found for the adjusted analysis. This finding was adjusted for age-by-degreasing chemical exposure (p=0.028). Group differences were assessed for each level of insecticide exposure to explore the interaction. As seen in Table H-2, the group relative risk was significantly greater than 1 for participants who had never been exposed to insecticides (Adj. RR: 2.17, 95% C.I.: [1.03,4.57], p=0.043). Conversely, it was marginally significantly less than 1 for participants who had been exposed to insecticides (Adj. RR: 0.64, 95% C.I.: [0.39,1.04], p=0.073).

Physical Examination Variables: Peripheral Nerve Status

Eight variables were analyzed to assess peripheral nerve status: pin prick, light touch, muscle status, vibration, patellar reflex, Achilles reflex, biceps reflex, and Babinski reflex. Unadjusted and adjusted results are summarized in Tables 11-6 and 11-7, respectively. Because of the low number of abnormalities, adjusted analyses were not done for the biceps and Babinski reflexes.

Pin Prick

Without adjustment for covariates, the prevalence of pin prick abnormalities was not significantly different between groups (p=0.902).

Using pooled group data, the covariate tests of association showed that age (p=0.014) and diabetic class (p<0.001) were significantly associated with pin prick abnormality. The percentage of abnormalities increased with age (4.6%, 7.4%, and 9.2% for individuals born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). Of the diabetic classes, diabetics had a much higher abnormal response rate (14.9%) than either impaired individuals (4.8%) or normal individuals (5.5%).

The group difference remained nonsignificant (p=0.958) after adjusting for age (p=0.002) and diabetic class (p<0.001).

TABLE 11-6.

Unadjusted Analysis for Peripheral Nerve Status Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Pin Prick	n	971		1,264			
	Number/%						
	Abnormal	62	6.4%	78	6.2%	1.04 (0.74,1.46)	0.902
	Normal	909	93.6%	1,186	93.8%		
Light Touch	n	971		1,263			
	Number/%						
	Abnormal	44	4.5%	57	4.5%	1.00 (0.67,1.50)	0.999
	Normal	927	95.5%	1,206	95.5%		
Muscle Status	n	991		1,291			
	Number/%						
	Abnormal	24	2.4%	26	2.0%	1.21 (0.69,2.12)	0.604
	Normal	967	97.6%	1,265	98.0%		
Vibration	n	971		1,263			
	Number/%						
	Abnormal	18	1.9%	17	1.3%	1.38 (0.71,2.70)	0.430
	Normal	953	98.1%	1,246	98.7%		
Patellar Reflex	n	993		1,291			
	Number/%						
	Abnormal	16	1.6%	21	1.6%	0.99 (0.51,1.91)	0.999
	Normal	977	98.4%	1,270	98.4%		
Achilles Reflex	n	991		1,292			
	Number/%						
	Abnormal	57	5.8%	78	6.0%	0.95 (0.67,1.35)	0.846
	Normal	934	94.2%	1,214	94.0%		

TABLE 11-6. (continued)

Unadjusted Analysis for Peripheral Nerve Status Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Biceps Reflex	n	993		1,294			
	Number/%						
	Abnormal	2	0.2%	15	1.2%	0.17 (0.04,0.75)	0.012
	Normal	991	99.8%	1,279	98.8%		
Babinski Reflex	n	993		1,292			
	Number/%						
	Abnormal	5	0.5%	4	0.3%	1.63 (0.44,6.08)	0.684
	Normal	988	99.5%	1,288	99.7%		

TABLE 11-7.

Adjusted Analysis for Peripheral Nerve Status Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Pin Prick	n	966	1,257	1.01 (0.71,1.43)	0.958	AGE (p=0.002) DIAB (p<0.001)
Light Touch	n	956	1,253	0.98 (0.65,1.48)	0.925	AGE*RACE (p=0.044) OCC*DIAB (p=0.005) AGE*DRKYR (p=0.047)
Muscle Status	n	991	1,291	1.17 (0.66,2.07)	0.596	AGE*INS (p=0.007)
Vibration	n	966	1,256	1.44 (0.73,2.86)**	0.293**	GRP*DIAB (p=0.042) AGE*INS (p=0.006)
Patellar Reflex	n	988	1,284	0.97 (0.50,1.89)	0.932	DIAB (p<0.001) AGE*OCC (p=0.016)
Achilles Reflex	n	986	1,285	0.84 (0.58,1.22)	0.350	AGE (p<0.001) RACE*DIAB (p=0.030) RACE*INS (p=0.019)

**Group-by-covariate interaction ($0.01<p\leq0.05$)--adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

Light Touch

Without covariate adjustment, the percentage of abnormal light touch responses was essentially the same between groups (p=0.999).

Diabetic class was the only covariate significantly associated with light touch (p<0.001). The percentages of abnormalities were 3.6 percent, 4.8 percent, and 11.9 percent for the normal, impaired, and diabetic classes, respectively.

The adjusted relative risk was not significant (p=0.925). Age-by-race (p=0.044), occupation-by-diabetic class (p=0.005), and age-by-lifetime alcohol history (p=0.047) interactions were used for adjustment.

Muscle Status

In the unadjusted analysis, the prevalence of abnormal muscle status was not significantly different between the Ranch Hand and Comparison groups (p=0.604).

Muscle status was associated with age (p=0.008), diabetic class (p=0.009), and lifetime alcohol history (p=0.037). The percentage of abnormalities increased with age (1.4%, 2.6%, and 6.1% for participants born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). Of the diabetic classes, the highest percentage of abnormalities was found for diabetics (5.1%), followed by normal individuals (2.0%) and impaired individuals (1.6%). The percentages of abnormalities were 2.9 percent, 1.7 percent, and 3.5 percent for men who had never drunk, for drinkers with up to 40 drink-years, and for drinkers with more than 40 drink-years, respectively.

The group difference remained nonsignificant (p=0.596) after adjusting for an age-by-insecticide exposure interaction (p=0.007).

Vibration

The percentage of vibration abnormalities did not differ significantly between groups (p=0.430) in the unadjusted analysis.

Age (p<0.001), diabetic class (p=0.035), and lifetime alcohol history (p=0.032) were associated with vibration. The percentage of abnormalities increased with age (0.9%, 1.7%, and 7.9% for participants born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). For diabetic class, diabetics had relatively more abnormalities (3.5%) than either normal (1.5%) or impaired individuals (0.7%). The percentage of vibration abnormalities exhibited an increasing trend with lifetime alcohol history (0.5%, 1.3%, and 2.8% for the 0, >0-40, and >40 drink-years categories, respectively).

A significant group-by-diabetic class interaction was found for the adjusted analysis (p=0.042). An age-by-insecticide exposure interaction (p=0.006) was used for adjustment. Group differences were assessed for each

level of diabetic class to explain the interaction. For this analysis, the impaired and diabetic categories were collapsed because there were only two abnormalities for the impaired category (both were Comparisons). As seen in Table H-2, these analyses revealed a marginally significant group difference for normal participants (Adj. RR: 2.16, 95% C.I.: [0.95,4.93], p=0.067). By contrast, the adjusted relative risk was less than 1, but not significant for impaired and diabetic participants (Adj. RR: 0.34, 95% C.I.: [0.07,1.66], p=0.180). No significant group difference was found (p=0.293) after excluding the group-by-diabetic class interaction and adjusting for age-by-insecticide exposure.

Patellar Reflex

Without covariate adjustment, the prevalence of patellar reflex abnormalities was not significantly different between groups (p=0.999).

The patellar reflex was significantly associated with diabetic class (p<0.001) and lifetime alcohol history (p=0.012). A marginally significant association with age (p=0.093) was also found. The percentages of abnormalities were 1.3 percent, 0.6 percent, and 5.5 percent for normal, impaired, and diabetic individuals, respectively. The relationship with lifetime alcohol history was not linear. Moderate drinkers had relatively fewer abnormalities (1.1% for individuals with >0-40 drink-years) than either heavy drinkers (2.9% for men with >40 drink-years) or participants who had never drunk (2.5%). A mild, increasing association with age was seen. The percentages of abnormalities were 0.9 percent, 2.1 percent, and 2.4 percent for individuals born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively.

No significant group difference was found in the adjusted analysis (p=0.932). This finding was adjusted for diabetic class (p<0.001) and the age-by-occupation (p=0.016) interaction.

Achilles Reflex

The group difference for the unadjusted analysis was not significant for the Achilles reflex (p=0.846).

The Achilles reflex was associated with age (p<0.001), diabetic class (p<0.001), and lifetime alcohol history (p=0.003). The prevalence of an abnormal Achilles reflex increased with age (2.0%, 8.1%, and 18.1% for participants born in or after 1942, for those born between 1923 and 1941, and for those born in or before 1922, respectively). Relatively more diabetics had an abnormal Achilles reflex (18.4%) than either impaired individuals (5.7%) or normal individuals (4.4%). Of the lifetime alcohol history categories, participants with more than 40 drink-years had the most abnormalities (8.5%), and moderate drinkers had the fewest abnormalities (4.8% for participants with >0-40 drink-years); individuals who had never drunk fell in between (7.8%).

No significant group difference was found in the adjusted analysis (p=0.350). Age (p<0.001), race-by-diabetic class (p=0.030), and race-by-insecticide exposure (p=0.019) contributed to the model.

Biceps Reflex

The percentage of Ranch Hands with an abnormal biceps reflex was significantly less than the corresponding percentage of Comparisons in the unadjusted analysis (Est. RR: 0.17, 95% C.I.: [0.04,0.75], p=0.012]. Fifteen Comparisons (1.2%) had an abnormal biceps reflex in contrast to only two Ranch Hands (0.2%).

Babinski Reflex

No significant group difference was noted for the Babinski reflex (p=0.684) in the unadjusted analysis.

Physical Examination Variables: CNS Coordination

Tremor, coordination, Romberg sign, gait, and an overall summary index constructed from these four variables were analyzed to assess CNS coordination processes. Unadjusted group contrasts were done for each variable; results are given in Table 11-8. Adjusted analyses were done for all variables except the Romberg sign, which had too few abnormals for adjustment; Table 11-9 presents the results.

Tremor

The unadjusted group difference was not significant (p=0.176).

The covariate tests of association detected a significant relationship between tremor and lifetime alcohol history (p=0.038). The percentage of abnormalities increased with drinking (1.5%, 2.6%, and 4.5% for participants with 0, >0 to 40, and >40 drink-years, respectively). None of the other candidate covariates was significantly associated with tremor.

No significant group difference was found in the adjusted analysis (p=0.110). The final model was adjusted for lifetime alcohol history (p=0.015) and an occupation-by-diabetic class interaction (p=0.037).

Coordination

The prevalence of coordination abnormalities was marginally significantly higher in the Ranch Hand group than in the Comparison group (Est. RR: 2.46, 95% C.I.: [1.04,5.83], p=0.058) in the unadjusted analysis.

Occupation was marginally associated with coordination (p=0.099). The percentages of coordination abnormalities were 0.5 percent, 1.0 percent, and 1.5 percent for the officer, enlisted flyer, and enlisted groundcrew cohorts, respectively.

The adjusted analysis detected two significant group-by-covariate interactions: group-by-occupation (p=0.014) and group-by-insecticide exposure (p=0.041). Age (p=0.004) and an occupation-by-insecticide exposure interaction (p=0.002) were used for adjustment. Followup investigation of these

TABLE 11-8.

Unadjusted Analysis for CNS Coordination Variables by Group

Variable	Statistic	Group: Ranch Hand		Group: Comparison		Est. Relative Risk (95% C.I.)	p-Value
Tremor	n	993		1,294			
	Number/%						
	Abnormal	35	3.5%	32	2.5%	1.44 (0.89,2.34)	0.176
	Normal	958	96.5%	1,262	97.5%		
Coordination	n	992		1,291			
	Number/%						
	Abnormal	15	1.5%	8	0.6%	2.46 (1.04,5.83)	0.058
	Normal	977	98.5%	1,283	99.4%		
Romberg Sign	n	993		1,292			
	Number/%						
	Abnormal	4	0.4%	0	0.0%	--	0.072
	Normal	989	99.6%	1,292	100.0%		
Gait	n	992		1,292			
	Number/%						
	Abnormal	32	3.2%	34	2.6%	1.23 (0.76,2.01)	0.474
	Normal	960	96.8%	1,258	97.4%		
CNS Index	n	992		1,291			
	Number/%						
	Abnormal	66	6.7%	64	5.0%	1.37 (0.96,1.95)	0.102
	Normal	926	93.3%	1,227	95.0%		

TABLE 11-9.

Adjusted Analysis for CNS Coordination Variables by Group

Variable	Statistic	Group		Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
		Ranch Hand	Comparison			
Tremor	n	978	1,284	1.50 (0.91,2.47)	0.110	DRKYR (p=0.015) OCC*DIAB (p=0.037)
Coordination	n	992	1,291	2.49 (1.04,6.00)**	0.036**	GRP*OCC (p=0.014) GRP*INS (p=0.041) AGE (p=0.004) OCC*INS (p=0.002)
Gait	n	982	1,289	1.21 (0.72,2.01)	0.474	AGE (p<0.001) DRKYR (p=0.006) OCC*INS (p=0.005)
CNS Index	n	982	1,288	1.34 (0.94,1.93)	0.109	AGE (p<0.001) OCC (p=0.002) DRKYR (p=0.008)

**Group-by-covariate interaction (0.01<p≤0.05)--adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

interactions involved separate adjusted analyses for each occupational cohort. As seen in Table H-2, these analyses found no significant group difference for either the officer cohort (Adj. RR: 3.92, 95% C.I.: [0.41,37.88], p=0.199) or the enlisted flyer cohort (Adj. RR: 0.33, 95% C.I.: [0.03,3.16], p=0.299). Insecticide exposure contributed to the enlisted flyer model. However, for the enlisted groundcrew cohort, a significant group-by-insecticide exposure interaction was found (p=0.040), after adjusting for age. Further stratification by insecticide exposure revealed a significant group difference for enlisted groundcrew exposed to insecticides (p=0.016). All seven coordination abnormalities in this subpopulation were from the Ranch Hand group. A significant group difference remained for the enlisted groundcrew after deleting the group-by-insecticide exposure interaction and adjusting for age (Adj. RR: 3.72, 95% C.I.: [1.17,11.81], p=0.017). A final adjusted analysis was done excluding both group-by-covariate interactions. This analysis showed a significant group difference overall (Adj. RR: 2.49, 95% C.I.: [1.04,6.00], p=0.036), adjusting for age and occupation-by-insecticide exposure (see Table 11-9).

Romberg Sign

In the unadjusted analysis, a marginally significant group difference was found for the Romberg sign (p=0.072). All four participants with an abnormal Romberg sign were Ranch Hands (this variable is identical to balance, discussed previously under cranial nerve function). Covariate tests of association and an adjusted analysis were not done because there were few abnormalities.

Gait

The percentage of gait abnormalities did not differ significantly between groups (p=0.474) in the unadjusted analysis.

Using pooled group data, occupation (p=0.033) and lifetime alcohol history (p=0.001) were significantly associated with gait. A marginal association with diabetic class was also found (p=0.074). The highest percentage of gait abnormalities was found for the enlisted groundcrew cohort (3.7%), followed by the enlisted flyer (3.4%) and the officer (1.7%) cohorts. The association with lifetime alcohol history was not linear. Relatively fewer gait abnormalities were found for moderate lifetime drinkers (1.9% for >0-40 drink-years) than for either heavy drinkers (4.7% for >40 drink-years) or for men who had never drunk (4.9%). For diabetic class, the percentages of abnormalities were 2.4 percent, 3.1 percent, and 5.1 percent for the normal, impaired, and diabetic categories, respectively.

The group difference remained nonsignificant (p=0.474) after adjusting for age (p<0.001), lifetime alcohol history (p=0.006), and occupation-by-insecticide exposure (p=0.005).

CNS Index

No significant unadjusted group difference was found for the CNS index (p=0.102).

The CNS index was significantly associated with lifetime alcohol history ($p=0.001$) and marginally associated with occupation ($p=0.066$) and diabetic class ($p=0.094$). Of the lifetime alcohol history categories, the highest percentage of abnormalities was found for heavy drinkers (8.7% for men with >40 drink-years), followed by men who had never drunk (6.4%) and moderate drinkers (4.5% for men with >0 to 40 drink-years). The percentages of abnormalities were 4.4 percent, 5.5 percent, and 6.9 percent for the officer, enlisted flyer, and enlisted groundcrew cohorts, respectively. For diabetic class, relatively more abnormalities were found for diabetic individuals (8.8%) than for either normal (5.2%) or impaired (5.0%) individuals.

The adjusted analysis did not detect a significant group difference ($p=0.109$). Age ($p<0.001$), occupation ($p=0.002$), and lifetime alcohol history ($p=0.008$) were used for adjustment.

Exposure Index Analysis

Unadjusted differences among exposure categories were assessed for all physical examination variables discussed above. Corresponding results are presented in Table 11-10. Adjusted exposure index analyses were done only for those variables for which adjusted Ranch and Comparison group contrasts were also done. Results for these analyses are presented in Table 11-11. Exposure index-by-covariate interactions are listed in Table 11-12, and stratified results are shown in Table H-3. The final interpretation of these exposure index data must await the reanalysis of the clinical data using the results of the serum dioxin assay. The report is expected in 1991.

Physical Examination Variables: Cranial Nerve Function

For each occupational cohort, no significant unadjusted results were noted for any of the 17 variables analyzed to assess the association between the exposure index and cranial nerve function. However, for many analyses, the statistical power needed to detect a statistically significant result was limited by the low prevalence rate of abnormal responses.

Adjusted exposure index analyses were done for palpebral fissure, neck range of motion, and two cranial nerve function summary indices. As shown in Table 11-12, a significant exposure index-by-age interaction was found for palpebral fissure in the enlisted groundcrew cohort, and also for the cranial nerve index without neck range of motion for the officer cohort. Stratified analyses to explore these interactions revealed no significant findings. All other adjusted analyses supported the unadjusted analyses, yielding no significant results.

Physical Examination Variables: Peripheral Nerve Status

The unadjusted analyses found no significant associations between the exposure index and eight peripheral nerve status variables (pin prick, light touch, muscle status, vibration, patellar reflex, Achilles reflex, biceps reflex, and Babinski reflex) in each occupational cohort.

TABLE 11-10.

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Smell	Officer	n	130		122		125		Overall		0.999
		Number/%									
		Abnormal	1	0.8%	1	0.8%	1	0.8%	M vs. L	1.07 (0.07,17.23)	0.999
		Normal	129	99.2%	121	99.2%	124	99.2%	H vs. L	1.04 (0.06,16.82)	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.612
		Number/%									
		Abnormal	0	0.0%	1	1.6%	1	1.9%	M vs. L	--	0.999
		Normal	55	100.0%	62	98.4%	52	98.1%	H vs. L	--	0.982
	Enlisted Groundcrew	n	147		158		140		Overall		0.629
		Number/%									
		Abnormal	1	0.7%	1	0.6%	0	0.0%	M vs. L	0.93 (0.06,15.00)	0.999
		Normal	146	99.3%	157	99.4%	140	100.0%	H vs. L	--	0.999
Visual Fields	Officer	n	130		122		125		Overall		--
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	--	--
		Normal	130	100.0%	122	100.0%	125	100.0%	H vs. L	--	--
	Enlisted Flyer	n	55		63		53		Overall		0.346
		Number/%									
		Abnormal	1	1.8%	0	0.0%	0	0.0%	M vs. L	--	0.932
		Normal	54	98.2%	63	100.0%	53	100.0%	H vs. L	--	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.362
		Number/%									
		Abnormal	1	0.7%	0	0.0%	0	0.0%	M vs. L	--	0.964
		Normal	146	99.3%	158	100.0%	140	100.0%	H vs. L	--	0.999

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Light Reaction	Officer	n	130		122		125		Overall		0.384
		Number/%									
		Abnormal	2	1.5%	1	0.8%	0	0.0%	M vs. L	0.53 (0.05,5.91)	0.999
		Normal	128	98.5%	121	99.2%	125	100.0%	H vs. L	--	0.518
	Enlisted Flyer	n	55		63		53		Overall		--
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	--	--
		Normal	55	100.0%	63	100.0%	53	100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147		158		140		Overall		0.767
		Number/%									
		Abnormal	2	1.4%	1	0.6%	1	0.7%	M vs. L	0.46 (0.04,5.15)	0.946
		Normal	145	98.6%	157	99.4%	139	99.3%	H vs. L	0.52 (0.05,5.82)	0.999
Ocular Movement	Officer	n	130		122		125		Overall		0.589
		Number/%									
		Abnormal	0	0.0%	1	0.8%	1	0.8%	M vs. L	--	0.968
		Normal	130	100.0%	121	99.2%	124	99.2%	H vs. L	--	0.980
	Enlisted Flyer	n	55		63		53		Overall		0.346
		Number/%									
		Abnormal	1	1.8%	0	0.0%	0	0.0%	M vs. L	--	0.932
		Normal	54	98.2%	63	100.0%	53	100.0%	H vs. L	--	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.767
		Number/%									
		Abnormal	2	1.4%	1	0.6%	1	0.7%	M vs. L	0.46 (0.04,5.15)	0.946
		Normal	145	98.6%	157	99.4%	139	99.3%	H vs. L	0.52 (0.05,5.82)	0.999

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Facial Sensation	Officer	n	130	122	125	Overall		0.386
		Number/%						
		Abnormal	1 0.8%	0 0.0%	0 0.0%	M vs. L	--	0.999
		Normal	129 99.2%	122 100.0%	125 100.0%	H vs. L	--	0.999
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.394
		Number/%						
		Abnormal	2 1.4%	2 1.3%	0 0.0%	M vs. L	0.93 (0.13,6.69)	0.999
		Normal	145 98.6%	156 98.7%	140 100.0%	H vs. L	--	0.522
Jaw Clench	Officer	n	130	122	125	Overall		0.386
		Number/%						
		Deviated	1 0.8%	0 0.0%	0 0.0%	M vs. L	--	0.999
		Symmetric	129 99.2%	122 100.0%	125 100.0%	H vs. L	--	0.999
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Deviated	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Symmetric	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.402
		Number/%						
		Deviated	0 0.0%	1 0.6%	0 0.0%	M vs. L	--	0.999
		Symmetric	147 100.0%	157 99.4%	140 100.0%	H vs. L	--	--

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low		Exposure Index Medium		Exposure Index High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Smile	Officer	n	130		122		125		Overall		0.606
		Number/%									
		Abnormal	1	0.0%	1	0.8%	0	0.0%	M vs. L	1.07 (0.07,17.23)	0.999
		Normal	129	100.0%	121	99.2%	125	100.0%	H vs. L	--	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.422
		Number/%									
		Abnormal	0	0.0%	1	1.6%	0	0.0%	M vs. L	--	0.999
		Normal	55	100.0%	62	98.4%	53	100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147		158		140		Overall		0.365
		Number/%									
		Abnormal	0	0.0%	2	1.3%	2	1.4%	M vs. L	--	0.536
		Normal	147	100.0%	156	98.7%	138	98.6%	H vs. L	--	0.474
Palpebral Fissure	Officer	n	130		122		125		Overall		0.232
		Number/%									
		Abnormal	2	1.5%	3	2.5%	0	0.0%	M vs. L	1.61 (0.27,9.83)	0.940
		Normal	128	98.5%	119	97.5%	125	100.0%	H vs. L	--	0.518
	Enlisted Flyer	n	55		63		53		Overall		0.325
		Number/%									
		Abnormal	0	0.0%	1	1.6%	2	3.8%	M vs. L	--	0.999
		Normal	55	100.0%	62	98.4%	51	96.2%	H vs. L	--	0.476
	Enlisted Groundcrew	n	147		158		140		Overall		0.558
		Number/%									
		Abnormal	1	0.7%	2	1.3%	3	2.1%	M vs. L	1.87 (0.17,20.86)	0.999
		Normal	146	99.3%	156	98.7%	137	97.9%	H vs. L	3.20 (0.33,31.11)	0.586

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Balance	Officer	n	130	122	125	Overall		0.364
		Number/%						
		Abnormal	0 0.0%	0 0.0%	1 0.8%	M vs. L	--	--
		Normal	130 100.0%	122 100.0%	124 99.2%	H vs. L	--	0.980
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.996
		Number/%						
		Abnormal	1 0.7%	1 0.6%	1 0.7%	M vs. L	0.93 (0.06,15.00)	0.999
		Normal	146 99.3%	157 99.4%	139 99.3%	H vs. L	1.05 (0.07,16.96)	0.999
Gag Reflex	Officer	n	130	122	125	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	130 100.0%	122 100.0%	125 100.0%	H vs. L	--	--
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	146	158	140	Overall		0.404
		Number/%						
		Abnormal	0 0.0%	1 0.6%	0 0.0%	M vs. L	--	0.999
		Normal	146 100.0%	157 99.4%	140 100.0%	H vs. L	--	--

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Speech	Officer	n	130	122	125	Overall		0.364
		Number/%						
		Abnormal	0 0.0%	0 0.0%	1 0.8%	M vs. L	--	--
		Normal	130 100.0%	122 100.0%	124 99.2%	H vs. L	--	0.980
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.629
		Number/%						
		Abnormal	1 0.7%	1 0.6%	0 0.0%	M vs. L	0.93 (0.06,15.00)	0.999
		Normal	146 99.3%	157 99.4%	140 100.0%	H vs. L	--	0.999
Tongue Position Relative to Midline	Officer	n	130	122	125	Overall		0.386
		Number/%						
		Abnormal	1 0.8%	0 0.0%	0 0.0%	M vs. L	--	0.999
		Normal	129 99.2%	122 100.0%	125 100.0%	H vs. L	--	0.999
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.402
		Number/%						
		Abnormal	0 0.0%	1 0.6%	0 0.0%	M vs. L	--	0.999
		Normal	147 100.0%	157 99.4%	140 100.0%	H vs. L	--	--

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Palate and Uvula Movement	Officer	n	130	122	125	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	130 100.0%	122 100.0%	125 100.0%	H vs. L	--	--
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/%						
		Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.402
		Number/%						
		Abnormal	0 0.0%	1 0.6%	0 0.0%	M vs. L	--	0.999
		Normal	147 100.0%	157 99.4%	140 100.0%	H vs. L	--	--
Neck Range of Motion	Officer	n	130	122	125	Overall		0.319
		Number/%						
		Abnormal	17 13.1%	23 18.9%	16 12.8%	M vs. L	1.54 (0.78,3.06)	0.280
		Normal	113 86.9%	99 81.1%	109 87.2%	H vs. L	0.98 (0.47,2.03)	0.999
	Enlisted Flyer	n	55	63	53	Overall		0.645
		Number/%						
		Abnormal	8 14.5%	8 12.7%	10 18.9%	M vs. L	0.86 (0.30,2.45)	0.978
		Normal	47 85.5%	55 87.3%	43 81.1%	H vs. L	1.37 (0.49,3.78)	0.730
	Enlisted Groundcrew	n	147	158	140	Overall		0.127
		Number/%						
		Abnormal	14 9.5%	8 5.1%	16 11.4%	M vs. L	0.51 (0.21,1.25)	0.200
		Normal	133 90.5%	150 94.9%	124 88.6%	H vs. L	1.23 (0.57,2.62)	0.738

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Cranial Nerve Index	Officer	n	129		121		125		Overall		0.182
		Number/%									
		Abnormal	21	16.3%	27	22.3%	17	13.6%	M vs. L	1.48 (0.78,2.78)	0.294
		Normal	108	83.7%	94	77.7%	108	86.4%	H vs. L	0.81 (0.41,1.62)	0.674
	Enlisted Flyer	n	55		63		53		Overall		0.643
		Number/%									
		Abnormal	10	18.2%	10	15.9%	12	22.6%	M vs. L	0.85 (0.32,2.22)	0.928
		Normal	45	81.8%	53	84.1%	41	77.4%	H vs. L	1.32 (0.52,3.37)	0.736
	Enlisted Groundcrew	n	146		153		138		Overall		0.165
		Number/%									
		Abnormal	22	15.1%	13	8.5%	20	14.5%	M vs. L	0.52 (0.25,1.08)	0.112
		Normal	124	84.9%	140	91.5%	118	85.5%	H vs. L	0.96 (0.50,1.84)	0.999
Cranial Nerve Index Without Range of Motion	Officer	n	129		121		125		Overall		0.458
		Number/%									
		Abnormal	5	3.9%	5	4.1%	2	1.6%	M vs. L	1.07 (0.30,3.79)	0.999
		Normal	124	96.1%	116	95.9%	123	98.4%	H vs. L	0.40 (0.08,2.12)	0.472
	Enlisted Flyer	n	55		63		53		Overall		0.780
		Number/%									
		Abnormal	2	3.6%	2	3.2%	3	5.7%	M vs. L	0.87 (0.12,6.38)	0.999
		Normal	53	96.4%	61	96.8%	50	94.3%	H vs. L	1.59 (0.26,9.92)	0.964
	Enlisted Groundcrew	n	146		153		138		Overall		0.573
		Number/%									
		Abnormal	10	6.8%	7	4.6%	6	4.3%	M vs. L	0.65 (0.24,1.76)	0.550
		Normal	136	93.2%	146	95.4%	132	95.7%	H vs. L	0.62 (0.22,1.75)	0.514

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Pin Prick	Officer	n	130		120		120		Overall		0.288
		Number/%									
		Abnormal	12	9.2%	6	5.0%	6	5.0%	M vs. L	0.52 (0.19,1.43)	0.294
		Normal	118	90.8%	114	95.0%	114	95.0%	H vs. L	0.52 (0.19,1.43)	0.294
	Enlisted Flyer	n	52		62		52		Overall		0.968
		Number/%									
		Abnormal	3	5.8%	3	4.8%	3	5.8%	M vs. L	0.83 (0.16,4.30)	0.999
		Normal	49	94.2%	59	95.2%	49	94.2%	H vs. L	1.00 (0.19,5.20)	0.999
	Enlisted Groundcrew	n	144		155		136		Overall		0.681
		Number/%									
		Abnormal	11	7.6%	11	7.1%	7	5.1%	M vs. L	0.92 (0.39,2.20)	0.999
		Normal	133	92.4%	144	92.9%	129	94.9%	H vs. L	0.66 (0.25,1.75)	0.546
Light Touch	Officer	n	130		120		120		Overall		0.239
		Number/%									
		Abnormal	9	6.9%	3	2.5%	5	4.2%	M vs. L	0.35 (0.09,1.31)	0.178
		Normal	121	93.1%	117	97.5%	115	95.8%	H vs. L	0.59 (0.19,1.80)	0.504
	Enlisted Flyer	n	52		62		52		Overall		0.493
		Number/%									
		Abnormal	2	3.8%	1	1.6%	3	5.8%	M vs. L	0.41 (0.04,4.65)	0.868
		Normal	50	96.2%	61	98.4%	49	94.2%	H vs. L	1.53 (0.25,9.56)	0.999
	Enlisted Groundcrew	n	144		155		136		Overall		0.462
		Number/%									
		Abnormal	8	5.6%	9	5.8%	4	2.9%	M vs. L	1.05 (0.39,2.79)	0.999
		Normal	136	94.4%	146	94.2%	132	97.1%	H vs. L	0.52 (0.15,1.75)	0.434

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Muscle Status	Officer	n	130		122		125		Overall		0.404
		Number/%									
		Abnormal	5	3.8%	2	1.6%	2	1.6%	M vs. L	0.42 (0.08,2.19)	0.500
		Normal	125	96.2%	120	98.4%	123	98.4%	H vs. L	0.41 (0.08,2.14)	0.480
	Enlisted Flyer	n	55		62		53		Overall		0.850
		Number/%									
		Abnormal	1	1.8%	2	3.2%	1	1.9%	M vs. L	1.80 (0.16,20.41)	0.999
		Normal	54	98.2%	60	96.8%	52	98.1%	H vs. L	1.04 (0.06,17.04)	0.999
	Enlisted Groundcrew	n	146		158		140		Overall		0.378
		Number/%									
		Abnormal	2	1.4%	6	3.8%	3	2.1%	M vs. L	2.84 (0.56,14.31)	0.338
		Normal	144	98.6%	152	96.2%	137	97.9%	H vs. L	1.58 (0.26,9.58)	0.960
Vibration	Officer	n	130		120		120		Overall		0.769
		Number/%									
		Abnormal	4	3.1%	3	2.5%	2	1.7%	M vs. L	0.81 (0.18,3.69)	0.999
		Normal	126	96.9%	117	97.5%	118	98.3%	H vs. L	0.53 (0.10,2.97)	0.760
	Enlisted Flyer	n	52		62		52		Overall		0.109
		Number/%									
		Abnormal	0	0.0%	0	0.0%	2	3.8%	M vs. L	--	--
		Normal	52	100.0%	62	100.0%	50	96.2%	H vs. L	--	0.496
	Enlisted Groundcrew	n	144		155		136		Overall		0.617
		Number/%									
		Abnormal	3	2.1%	3	1.9%	1	0.7%	M vs. L	0.93 (0.18,4.67)	0.999
		Normal	141	97.9%	152	98.1%	135	99.3%	H vs. L	0.35 (0.04,3.39)	0.666

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Patellar Reflex	Officer	n	130		122		125		Overall		0.837
		Number/%									
		Abnormal	2	1.5%	1	0.8%	2	1.6%	M vs. L	0.53 (0.05,5.91)	0.999
		Normal	128	98.5%	121	99.2%	123	98.4%	H vs. L	1.04 (0.14,7.50)	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.612
		Number/%									
		Abnormal	0	0.0%	1	1.6%	1	1.9%	M vs. L	--	0.999
		Normal	55	100.0%	62	98.4%	52	98.1%	H vs. L	--	0.982
	Enlisted Groundcrew	n	147		158		140		Overall		0.763
		Number/%									
		Abnormal	2	1.4%	4	2.5%	3	2.1%	M vs. L	1.88 (0.34,10.44)	0.754
		Normal	145	98.6%	154	97.5%	137	97.9%	H vs. L	1.59 (0.26,9.65)	0.954
Achilles Reflex	Officer	n	130		122		125		Overall		0.473
		Number/%									
		Abnormal	10	7.7%	5	4.1%	7	5.6%	M vs. L	0.51 (0.17,1.55)	0.348
		Normal	120	92.3%	117	95.9%	118	94.4%	H vs. L	0.71 (0.26,1.93)	0.678
	Enlisted Flyer	n	55		63		53		Overall		0.172
		Number/%									
		Abnormal	4	7.3%	1	1.6%	5	9.4%	M vs. L	0.21 (0.02,1.90)	0.286
		Normal	51	92.7%	62	98.4%	48	90.6%	H vs. L	1.33 (0.34,5.24)	0.952
	Enlisted Groundcrew	n	145		158		140		Overall		0.225
		Number/%									
		Abnormal	10	6.9%	11	7.0%	4	2.9%	M vs. L	1.01 (0.42,2.45)	0.999
		Normal	135	93.1%	147	93.0%	136	97.1%	H vs. L	0.40 (0.12,1.30)	0.190

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low	Exposure Index: Medium	Exposure Index: High	Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Biceps Reflex	Officer	n	130	122	125	Overall		0.364
		Number/% Abnormal	0 0.0%	1 0.8%	0 0.0%	M vs. L	--	0.968
		Normal	130 100.0%	121 99.2%	125 100.0%	H vs. L	--	--
	Enlisted Flyer	n	55	63	53	Overall		--
		Number/% Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	55 100.0%	63 100.0%	53 100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147	158	140	Overall		0.362
		Number/% Abnormal	1 0.7%	0 0.0%	0 0.0%	M vs. L	--	0.964
		Normal	146 99.3%	158 100.0%	140 100.0%	H vs. L	--	0.999
Babinski Reflex	Officer	n	130	122	125	Overall		--
		Number/% Abnormal	0 0.0%	0 0.0%	0 0.0%	M vs. L	--	--
		Normal	130 100.0%	122 100.0%	125 100.0%	H vs. L	--	--
	Enlisted Flyer	n	55	63	53	Overall		0.346
		Number/% Abnormal	1 1.8%	0 0.0%	0 0.0%	M vs. L	--	0.932
		Normal	54 98.2%	63 100.0%	53 100.0%	H vs. L	--	0.999
	Enlisted Groundcrew	n	147	158	140	Overall		0.767
		Number/% Abnormal	2 1.4%	1 0.6%	1 0.7%	M vs. L	0.46 (0.04,5.15)	0.946
		Normal	145 98.6%	157 99.4%	139 99.3%	H vs. L	0.52 (0.05,5.82)	0.999

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Medium		High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Tremor	Officer	n	130		122		125		Overall		0.678
		Number/%									
		Abnormal	3	2.3%	3	2.5%	5	4.0%	M vs. L	1.07 (0.21,5.39)	0.999
		Normal	127	97.7%	119	97.5%	120	96.0%	H vs. L	1.76 (0.41,7.54)	0.680
	Enlisted Flyer	n	55		63		53		Overall		0.855
		Number/%									
		Abnormal	2	3.6%	2	3.2%	1	1.9%	M vs. L	0.87 (0.12,6.38)	0.999
		Normal	53	96.4%	61	96.8%	52	98.1%	H vs. L	0.51 (0.05,5.79)	0.999
	Enlisted Groundcrew	n	147		158		140		Overall		0.319
		Number/%									
		Abnormal	8	5.4%	8	5.1%	3	2.1%	M vs. L	0.93 (0.34,2.54)	0.999
		Normal	139	94.6%	150	94.9%	137	97.9%	H vs. L	0.38 (0.10,1.46)	0.250
Coordination	Officer	n	130		122		125		Overall		0.999
		Number/%									
		Abnormal	1	0.8%	1	0.8%	1	0.8%	M vs. L	1.07 (0.07,17.23)	0.999
		Normal	129	99.2%	121	99.2%	124	99.2%	H vs. L	1.04 (0.06,16.82)	0.999
	Enlisted Flyer	n	55		63		53		Overall		0.346
		Number/%									
		Abnormal	1	1.8%	0	0.0%	0	0.0%	M vs. L	--	0.932
		Normal	54	98.2%	63	100.0%	53	100.0%	H vs. L	--	0.999
	Enlisted Groundcrew	n	146		158		140		Overall		0.786
		Number/%									
		Abnormal	3	2.1%	5	3.2%	3	2.1%	M vs. L	1.56 (0.37,6.64)	0.812
		Normal	143	97.9%	153	96.8%	137	97.9%	H vs. L	1.04 (0.21,5.26)	0.999

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
Romberg Sign	Officer	n	130		122		125		Overall		0.364
		Number/%									
		Abnormal	0	0.0%	0	0.0%	1	0.8%	M vs. L	--	--
		Normal	130	100.0%	122	100.0%	124	99.2%	H vs. L	--	0.980
	Enlisted Flyer	n	55		63		53		Overall		--
		Number/%									
		Abnormal	0	0.0%	0	0.0%	0	0.0%	M vs. L	--	--
		Normal	55	100.0%	63	100.0%	53	100.0%	H vs. L	--	--
	Enlisted Groundcrew	n	147		158		140		Overall		0.996
		Number/%									
		Abnormal	1	0.7%	1	0.6%	1	0.7%	M vs. L	0.93 (0.06,15.00)	0.999
		Normal	146	99.3%	157	99.4%	139	99.3%	H vs. L	1.05 (0.07,16.96)	0.999
Gait	Officer	n	130		122		125		Overall		0.362
		Number/%									
		Abnormal	2	1.5%	1	0.8%	4	3.2%	M vs. L	0.53 (0.05,5.91)	0.999
		Normal	128	98.5%	121	99.2%	121	96.8%	H vs. L	2.12 (0.38,11.76)	0.648
	Enlisted Flyer	n	55		63		53		Overall		0.983
		Number/%									
		Abnormal	2	3.6%	2	3.2%	2	3.8%	M vs. L	0.87 (0.12,6.38)	0.999
		Normal	53	96.4%	61	96.8%	51	96.2%	H vs. L	1.04 (0.14,7.66)	0.999
	Enlisted Groundcrew	n	146		158		140		Overall		0.871
		Number/%									
		Abnormal	6	4.1%	6	3.8%	7	5.0%	M vs. L	0.92 (0.29,2.92)	0.999
		Normal	140	95.9%	152	96.2%	133	95.0%	H vs. L	1.23 (0.40,3.75)	0.938

TABLE 11-10. (continued)

Unadjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index: Low		Exposure Index: Medium		Exposure Index: High		Exposure Index Contrast	Est. Relative Risk (95% C.I.)	p-Value
CNS Index	Officer	n	130		122		125		Overall		0.449
		Number/%									
		Abnormal	5	3.8%	4	3.3%	8	6.4%	M vs. L	0.85 (0.22,3.23)	0.999
		Normal	125	96.2%	118	96.7%	117	93.6%	H vs. L	1.71 (0.54,5.37)	0.522
	Enlisted Flyer	n	55		63		53		Overall		0.976
		Number/%									
		Abnormal	3	5.5%	4	6.3%	3	5.7%	M vs. L	1.18 (0.25,5.50)	0.999
		Normal	52	94.5%	59	93.7%	50	94.3%	H vs. L	1.04 (0.20,5.40)	0.999
	Enlisted Groundcrew	n	146		158		140		Overall		0.874
		Number/%									
		Abnormal	14	9.6%	14	8.9%	11	7.9%	M vs. L	0.92 (0.42,2.00)	0.982
		Normal	132	90.4%	144	91.1%	129	92.1%	H vs. L	0.80 (0.35,1.84)	0.758

--Estimated relative risk, confidence interval, and p-value not given due to cell with zero frequency.

Note: Small sample sizes may affect validity of overall p-value.

TABLE 11-11.

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Palpebral Fissure	Officer	n	129	120	123	Overall		0.243
						M vs. L	0.84 (0.11,6.51)	0.871
						H vs. L	--	--
	Enlisted Flyer	n	54	62	53	Overall		0.166
						M vs. L	--	--
						H vs. L	--	--
	Enlisted Groundcrew	n	143	156	138	Overall		0.677**
						M vs. L	2.04 (0.17,24.11)**	0.571**
						H vs. L	2.66 (0.26,26.93)**	0.409**
Neck Range of Motion	Officer	n	129	120	123	Overall		0.781
						M vs. L	1.12 (0.54,2.36)	0.756
						H vs. L	0.86 (0.39,1.88)	0.706
	Enlisted Flyer	n	54	62	53	Overall		0.613
						M vs. L	0.89 (0.27,2.97)	0.855
						H vs. L	1.51 (0.51,4.48)	0.454
	Enlisted Groundcrew	n	143	156	138	Overall		0.631
						M vs. L	0.63 (0.24,1.65)	0.351
						H vs. L	0.89 (0.38,2.07)	0.788

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index			Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
			Low	Medium	High			
Cranial Nerve Index	Officer	n	128	119	123	Overall		0.507
						M vs. L	1.01 (0.50,2.02)	0.981
						H vs. L	0.69 (0.33,1.45)	0.326
	Enlisted Flyer	n	54	62	53	Overall		0.640
						M vs. L	0.95 (0.32,2.81)	0.921
						H vs. L	1.48 (0.54,4.04)	0.441
	Enlisted Groundcrew	n	142	151	136	Overall		0.423
						M vs. L	0.60 (0.28,1.30)	0.196
						H vs. L	0.78 (0.38,1.58)	0.490
Cranial Nerve Index Without Range of Motion	Officer	n	128	119	123	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Flyer	n	54	62	53	Overall		0.849
						M vs. L	1.13 (0.15,8.76)	0.909
						H vs. L	1.68 (0.26,10.98)	0.589
	Enlisted Groundcrew	n	142	151	136	Overall		0.483
						M vs. L	0.69 (0.25,1.91)	0.471
						H vs. L	0.52 (0.18,1.55)	0.243

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Pin Prick	Officer	n	129	118	118	Overall		0.121
						M vs. L	0.40 (0.13,1.18)	0.096
						H vs. L	0.38 (0.13,1.13)	0.083
	Enlisted Flyer	n	51	61	52	Overall		0.901
						M vs. L	0.73 (0.12,4.33)	0.726
						H vs. L	1.08 (0.19,6.05)	0.930
	Enlisted Groundcrew	n	140	153	134	Overall		****
						M vs. L	****	****
						H vs. L	****	****
Light Touch	Officer	n	129	118	118	Overall		0.043
						M vs. L	0.18 (0.04,0.81)	0.025
						H vs. L	0.36 (0.10,1.25)	0.106
	Enlisted Flyer	n	51	61	52	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Groundcrew	n	140	153	134	Overall		0.432**
						M vs. L	0.92 (0.33,2.59)**	0.875**
						H vs. L	0.47 (0.14,1.64)**	0.238**

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Muscle Status	Officer	n	129	120	123	Overall		0.210
						M vs. L	0.23 (0.04,1.40)	0.112
						H vs. L	0.37 (0.06,2.09)	0.259
	Enlisted Flyer	n	54	61	53	Overall		0.828**
						M vs. L	2.76 (0.10,79.89)**	0.554**
						H vs. L	1.15 (0.04,34.89)**	0.938**
	Enlisted Groundcrew	n	142	156	138	Overall		0.133**
						M vs. L	4.26 (0.77,23.67)**	0.098**
						H vs. L	1.20 (0.18,7.87)**	0.847**
Vibration	Officer	n	129	118	118	Overall		0.660
						M vs. L	0.54 (0.11,2.70)	0.449
						H vs. L	0.49 (0.08,3.01)	0.438
	Enlisted Flyer	n	51	61	52	Overall		--
						M vs. L	--	--
						H vs. L	--	--
	Enlisted Groundcrew	n	140	153	134	Overall		0.678
						M vs. L	1.57 (0.23,10.73)	0.647
						H vs. L	0.58 (0.05,7.00)	0.668

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Patellar Reflex	Officer	n	129	120	123	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Flyer	n	54	62	53	Overall		--
						M vs. L	--	--
						H vs. L	--	--
	Enlisted Groundcrew	n	143	156	138	Overall		0.778
						M vs. L	1.82 (0.30,10.91)	0.512
						H vs. L	1.19 (0.19,7.63)	0.851
Achilles Reflex	Officer	n	129	120	123	Overall		0.049
						M vs. L	0.23 (0.06,0.80)	0.021
						H vs. L	0.43 (0.14,1.33)	0.142
	Enlisted Flyer	n	54	62	53	Overall		0.187
						M vs. L	0.24 (0.02,2.82)	0.257
						H vs. L	1.67 (0.35,8.08)	0.522
	Enlisted Groundcrew	n	143	156	138	Overall		0.018
						M vs. L	1.40 (0.50,3.90)	0.516
						H vs. L	0.25 (0.07,0.96)	0.843

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Tremor	Officer	n	129	120	123	Overall		0.634
						M vs. L	0.76 (0.14,4.11)	0.747
						H vs. L	1.55 (0.35,6.90)	0.567
	Enlisted Flyer	n	54	62	53	Overall		0.993
						M vs. L	1.14 (0.08,16.64)	0.923
						H vs. L	0.97 (0.06,16.69)	0.985
	Enlisted Groundcrew	n	143	156	138	Overall		0.274
						M vs. L	0.95 (0.34,2.67)	0.927
						H vs. L	0.38 (0.10,1.48)	0.162
Coordi-nation	Officer	n	129	120	123	Overall		0.997
						M vs. L	0.95 (0.06,15.74)	0.969
						H vs. L	1.05 (0.06,17.52)	0.972
	Enlisted Flyer	n	54	62	53	Overall		--
						M vs. L	--	--
						H vs. L	--	--
	Enlisted Groundcrew	n	142	156	138	Overall		0.485**
						M vs. L	1.93 (0.43,8.57)**	0.389**
						H vs. L	0.78 (0.14,4.26)**	0.778**

TABLE 11-11. (continued)

Adjusted Exposure Index for Neurological Variables by Occupation

Variable	Occupation	Statistic	Exposure Index Low	Exposure Index Medium	Exposure Index High	Exposure Index Contrast	Adj. Relative Risk (95% C.I.)	p-Value
Gait	Officer	n	129	120	123	Overall		0.494
						M vs. L	0.41 (0.03,4.87)	0.482
						H vs. L	1.52 (0.24,9.64)	0.655
	Enlisted Flyer	n	54	62	53	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Groundcrew	n	142	156	138	Overall		0.908**
						M vs. L	1.05 (0.29,3.81)**	0.940**
						H vs. L	1.28 (0.39,4.26)**	0.682**
CNS Index	Officer	n	129	120	123	Overall		0.549**
						M vs. L	0.64 (0.16,2.57)**	0.525**
						H vs. L	1.29 (0.39,4.35)**	0.676**
	Enlisted Flyer	n	54	62	53	Overall		****
						M vs. L	****	****
						H vs. L	****	****
	Enlisted Groundcrew	n	142	156	138	Overall		0.887**
						M vs. L	0.98 (0.43,2.22)**	0.956**
						H vs. L	0.82 (0.35,1.93)**	0.652**

--Analysis not done due to sparse data.

**Exposure index-by-covariate interaction ($0.01<p\leq0.05$)--adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

****Exposure index-by-covariate interaction ($p\leq0.01$)--adjusted relative risk, confidence interval, and p-value not presented.

TABLE 11-12.

Summary of Exposure Index-by-Covariate Interactions from Adjusted Analyses for Neurological Variables*

Variable	Occupation	Covariate	p-Value
Palpebral Fissure	Enlisted Groundcrew	Age	0.049
Cranial Nerve Index Without Range of Motion	Officer	Age	<0.001
		Race	0.020
		Diabetic Class	0.014
Pin Prick	Enlisted Groundcrew	Insecticide Exposure	0.010
Light Touch	Enlisted Flyer	Age	0.009
		Diabetic Class	0.003
		Lifetime Alcohol History	0.006
Light Touch	Enlisted Groundcrew	Insecticide Exposure	0.027
Muscle Status	Enlisted Flyer	Age	0.031
Muscle Status	Enlisted Groundcrew	Diabetic Class	0.040
		Lifetime Alcohol History	0.043
Patellar Reflex	Officer	Age	0.023
		Diabetic Class	0.001
Coordination	Enlisted Groundcrew	Race	0.024
Gait	Enlisted Flyer	Age	<0.001
		Diabetic Class	0.044
		Lifetime Alcohol History	0.035
Gait	Enlisted Groundcrew	Lifetime Alcohol History	0.029
CNS Index	Officer	Age	0.018
CNS Index	Enlisted Flyer	Age	0.009
CNS Index	Enlisted Groundcrew	Age	0.033
		Lifetime Alcohol History	0.022

*Refer to Table H-3 for a further investigation of these interactions.

Significant or marginally significant adjusted results were found for pin prick, light touch, and the Achilles reflex for the officer cohort. However, the highest percentage of abnormalities for each variable was in the low exposure category. A significant overall result for Achilles reflex and a marginally significant medium versus low contrast for muscle status were found for the enlisted groundcrew. In neither case, however, was a dose-response relationship observed (the medium-exposed category had the most abnormalities).

As seen in Table 11-12, significant exposure index-by-covariate interactions were found for at least one variable for each cohort. Stratified analyses to explore these interactions found no significant results for the officer and enlisted flyer cohorts, but disclosed marginally significant results for pin prick and light touch for enlisted groundcrew who had never been exposed to insecticides. However, no evidence of a dose-response relationship was observed for either variable since the medium exposure category had the most abnormalities. All other adjusted results were not significant.

Physical Examination Variables: CNS Coordination

Unadjusted exposure results for each occupational cohort were not significant for tremor, coordination, Romberg sign, gait, and the CNS summary index.

Significant exposure index-by-covariate interactions were found for adjusted analyses of coordination, gait, and the CNS summary index, but stratified results were generally nonsignificant and did not support a herbicide effect. A significant result for the CNS index was found for enlisted groundcrew born in or after 1942 with more than 40 drink-years ($p=0.012$), but most of the abnormalities (five of seven) fell in the low exposure category. A marginally significant stratified result showed that the percentages of CNS index abnormalities increased with exposure for enlisted groundcrew who were born between 1923 and 1941 and had more than 0, but less than 40, drink-years ($p=0.080$). For all other adjusted analyses, no significant differences were detected among exposure categories.

Longitudinal Analysis

The cranial nerve index and the CNS index were investigated to assess longitudinal differences. Results from the 1985 followup examination were contrasted with the 1987 followup examination because SCRF conducted both of these neurological examinations. Table 11-13 presents summary statistics for the 1982 Baseline examination, the 1985 followup examination, and the 1987 followup examination. Results of the longitudinal analyses are seen in Table 11-14 and show that the group difference did not change significantly over time for each variable.

TABLE 11-13.

Summary Statistics for the Longitudinal Analysis of the Neurological Assessment: 1982 Baseline, 1985 Followup, and 1987 Followup Examinations

Variable	Examination	Statistic	Group			
			Ranch Hand		Comparison	
Cranial Nerve Index	1982 Baseline	n	855		1,028	
		Number/%				
		Abnormal	448	52.4%	537	52.2%
		Normal	407	47.6%	491	47.8%
	1985 Followup	n	939		1,187	
		Number/%				
		Abnormal	84	8.9%	99	8.3%
		Normal	855	91.1%	1,088	91.7%
	1987 Followup	n	939		1,187	
		Number/%				
		Abnormal	150	16.0%	174	14.7%
		Normal	789	84.0%	1,013	85.3%
CNS Index	1982 Baseline	n	907		1,074	
		Number/%				
		Abnormal	235	25.9%	293	27.3%
		Normal	672	74.1%	781	72.7%
	1985 Followup	n	957		1,214	
		Number/%				
		Abnormal	42	4.4%	36	3.0%
		Normal	915	95.6%	1,178	97.0%
	1987 Followup	n	957		1,214	
		Number/%				
		Abnormal	64	6.7%	61	5.0%
		Normal	893	93.3%	1,153	95.0%

Note: Summary statistics for the 1982 Baseline are based on participants who attended all three examinations and are included for reference purposes only. Summary statistics for the 1985 followup and the 1987 followup are for participants who attended both examinations.

TABLE 11-14.

Longitudinal Analysis for the Neurological Assessment: A Contrast of 1985 and 1987 Followup Examination Abnormalities

Variable	Group	1985 Followup Exam	1987 Followup Exam: Abnormal	1987 Followup Exam: Normal	Odds Ratio (OR)*	p-Value (OR_{RH} vs. OR_C)
Cranial Nerve Index	Ranch Hand	Abnormal	43	41	2.61	0.778
		Normal	107	748		
	Comparison	Abnormal	44	55	2.36	
		Normal	130	958		
CNS Index	Ranch Hand	Abnormal	21	21	2.05	0.999
		Normal	43	872		
	Comparison	Abnormal	9	27	1.93	
		Normal	52	1,126		

*Odds Ratio: $\frac{\text{Number Normal 1985 Followup, Abnormal 1987 Followup}}{\text{Number Abnormal 1985 Followup, Normal 1987 Followup}}$

DISCUSSION

Although definitive diagnosis usually requires laboratory testing beyond the scope of the current study, the data analyzed in the present section can be relied upon to detect the presence, if not the cause, of neurological disease. Of the clinical disciplines included in these examinations, the neurological assessment is by far the most complex and places a particular premium on meticulous detail in the performance of the physical examination. Pertinent to the current study, the neurological examination is highly sensitive in detecting the presence of peripheral neuropathy.

In practice, it is convenient to subdivide the neurological assessment into examinations of the peripheral and the cranial nerves. The 5 motor and 3 sensory peripheral nerve variables and the 12 cranial nerve variables can provide highly specific clues in the anatomic site of neurological lesions and clarify which additional diagnostic studies would be most helpful in establishing a diagnosis.

As indices of CNS function, tremor and coordination are far less specific and are more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extrapyramidal motor system disease as in Parkinson's syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position sense in the lower extremities or of inner ear disease. Finally, the mental status examination is of obvious importance in the CNS assessment and, as in previous examination cycles, extensive psychometric studies were conducted. These are reported in Chapter 12.

Most of the dependent variable-covariate associations documented in this chapter confirmed relationships that are well established in clinical practice. A decline in CNS function would be expected with advancing years, though individual variation is the rule and it is often impossible to sort out the effects of age from environmental and psychosocial factors. The gradual attrition of central and peripheral neurons over time is associated with diminished vibratory sensation in the lower extremities and reduction in the Achilles reflex, findings confirmed in the current study.

Diabetes mellitus was found to be associated with multiple manifestations of neurological disease, including deficits in pin prick, light touch, and vibratory sensation. Depending on the criteria applied, peripheral neuropathy will occur in up to 60 percent of diabetics and will increase in frequency with age and duration of disease. Though a single etiology of the sensory deficits in diabetes is unlikely, accelerated peripheral vascular disease with microangiopathy, common to all diabetics, is no doubt a contributing factor.

Alcohol abuse is classically associated with a wide range of central and peripheral neurological disorders, as confirmed in the current study. While acute inebriation is related to direct toxic effects on the central nervous system, a peripheral polyneuropathy solely attributable to the chronic effects of ethanol has not been demonstrated with certainty. Rather, the neurological complications of chronic alcohol abuse (e.g., Wernicke's disease, Korsokoff's psychosis, cerebellar ataxia, and polyneuropathy) appear to be different manifestations of a secondary nutritional deficiency.

Several of the neck range of motion covariate associations are difficult to explain clinically. The decrease in neck range of motion with age is associated with degenerative arthritis of the cervical spine and is usually painless. A minority of cases will be secondary to cervical disc disease and nerve root compression. In future examination cycles, the classification of neck range of motion as a neurological dependent variable will take into account the presence or absence of pain. The associations with race (nonblacks have more abnormalities than Blacks) and with diabetes were of uncertain cause and of doubtful clinical significance.

Of all the neurological variables examined, no clinically significant group differences were found. A small number of Ranch Hand participants (four) and no Comparisons were found to have an abnormal Romberg sign, an incidence of marginal statistical significance given the small numbers involved. Finally, the exposure index analyses failed to reveal any consistent trends suggestive of a dose-response relationship.

SUMMARY

The 1987 neurological assessment focused on extensive physical examination data for cranial nerve function, peripheral nerve status, and central nervous system coordination processes. Verified histories of neurological diseases were also examined. The statistical results for the Ranch Hand and Comparison group contrasts are summarized in Table 11-15.

Information from the questionnaire was verified and grouped into six categories of neurological diseases: inflammatory diseases, hereditary and degenerative diseases, peripheral disorders, disorders of the eye, disorders of the ear, and other neurological disorders. Unadjusted analyses found that Ranch Hands had a higher incidence of hereditary and degenerative diseases than Comparisons, but group differences for the other categories were not significant. Examples of hereditary and degenerative disease include Parkinson's disease and benign essential tremor, among others.

Seventeen variables were examined to assess group differences in cranial nerve function (smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, neck range of motion, the cranial nerve index, and the index without neck range of motion). No group difference was statistically significant, although the prevalence of balance abnormalities based on four cases was marginally higher for the Ranch Hand group than for the Comparison group. The adjusted analyses revealed a significant group-by-lifetime alcohol history interaction for palpebral fissure and a significant group-by-insecticide exposure interaction for the cranial nerve index without neck range of motion. Stratified results for the cranial nerve index without neck range of motion showed a relative risk significantly greater than 1 for participants who had never been exposed to insecticides and a relative risk marginally less than 1 for participants who had been exposed to insecticides. Stratified analyses for palpebral fissure failed to detect a significant group difference.

The variables analyzed to assess peripheral nerve status were pin prick, light touch, muscle status, vibration, patellar reflex, Achilles reflex,

TABLE 11-15.

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Neurological Variables

Variable	Unadjusted	Adjusted	Direction of Results
Questionnaire			
Inflammatory Disease	NS	--	
Hereditary and Degenerative Disease	0.030	--	
Peripheral Disorders	NS	--	
Disorders of the Eye	NS	--	
Disorders of the Ear	NS	--	
Other Neurological Disorders	NS	--	
Physical Examination: Cranial Nerve Function			
Smell	NS	--	
Visual Fields	NS	--	
Light Reaction	NS	--	
Ocular Movement	NS	--	
Facial Sensation	NS	--	
Jaw Clench	NS	--	
Smile	NS	--	
Palpebral Fissure	NS	** (NS)	
Balance	NS*	--	RH>C[a]
Gag Reflex	NS	--	
Speech	NS	--	
Tongue Position Relative to Midline	NS	--	
Palate and Uvula Movement	NS	--	
Neck Range of Motion	NS	NS	
Cranial Nerve Index	NS	NS	
Cranial Nerve Index Without Range of Motion	NS	****	
Physical Examination: Peripheral Nerve Status			
Pin Prick	NS	NS	
Light Touch	NS	NS	
Muscle Status	NS	NS	
Vibration	NS	** (NS)	
Patellar Reflex	NS	NS	
Achilles Reflex	NS	NS	
Biceps Reflex	0.012	--	C>RH
Babinski Reflex	NS	--	

TABLE 11-15. (continued)

Overall Summary Results of Unadjusted and Adjusted Group Contrast Analyses of Neurological Variables

Variable	Unadjusted	Adjusted	Direction of Results
Physical Examination: Central Nervous System Coordination Processes			
Tremor	NS	NS	
Coordination	NS*	** (0.036)	RH>C
Romberg Sign	NS*	--	RH>C[a]
Gait	NS	NS	
CNS Index	NS	NS	

NS: Not significant ($p>0.10$).

--Analysis not done.

** (NS): Group-by-covariate interaction ($0.01<p\leq0.05$); not significant when interaction is deleted; refer to Table H-2 for a detailed description of this interaction.

NS*: Borderline significant ($0.05<p\leq0.10$).

RH>C: More abnormalities in Ranch Hands.

****: Group-by-covariate interaction ($p\leq0.01$).

C>RH: More abnormalities in Comparisons.

** (0.036): Group-by-covariate interaction ($0.01<p\leq0.05$); significant when interaction is deleted; refer to Table H-2 for a detailed description of this interaction.

[a]Balance (Romberg sign).

biceps reflex, and Babinski reflex. The prevalence of biceps reflex abnormalities was significantly less for Ranch Hands than for Comparisons. The unadjusted group contrasts for the other variables were not significant. Results of the adjusted analyses were also not significant, except for a group-by-diabetic class interaction that was found for vibration. Exploration of this interaction showed that the adjusted relative risk was marginally greater than 1 for participants categorized as having normal glucose metabolism.

Tremor, coordination, Romberg sign (balance), gait, and the CNS summary index were analyzed to assess the central nervous system coordination processes. Unadjusted group contrasts revealed that Ranch Hands had marginally significantly more abnormalities than Comparisons for the Romberg sign and for coordination. The adjusted analysis for coordination detected two significant group-by-covariate interactions (group-by-occupation and group-by-insecticide exposure). Stratified analyses showed a significant group difference for enlisted groundcrew who had never been exposed to insecticides. Further investigation found a significant group difference for enlisted groundcrew after excluding the group-by-insecticide exposure interaction, and a significant adjusted group difference overall after excluding both group-by-covariate interactions. Ranch Hands had significantly more coordination abnormalities than Comparisons for each analysis.

Results for the exposure index analyses were generally not significant for each occupational cohort. Isolated significant findings did not indicate an effect due to herbicide exposure.

In conclusion, the 1987 neurological assessment did not find the health of the Ranch Hand group to be substantially different from the Comparison group, but several differences were noted. Of the questionnaire variables, Ranch Hands had a higher incidence of hereditary and degenerative diseases than Comparisons. Unadjusted analyses for the physical examination variables showed that Ranch Hands had marginally more abnormalities than Comparisons for balance/Romberg sign and coordination, but significantly fewer biceps reflex abnormalities. No significant group differences were detected for the other 26 physical examination variables.

CHAPTER 11

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